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10/648,536	08/25/2003	Robert Owen Lockerbie	B0175-US02	4649

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/648,536	LOCKERBIE ET AL.	
	Examiner	Art Unit	
	JAE W. LEE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/13/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 4-19 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-19 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

In response to the previous Office action, a Final rejection (mailed on 10/18/2007), Applicants filed an appeal brief received on 05/13/2008. Claims 2, 3 and 20 are canceled. Claims 1, 4-19 and 21-23 are pending. Upon further consideration, the finality of the previous Office action is hereby withdrawn and prosecution is reopened due to the introduction of new grounds of rejection. Claims 8 and 11-19 are rejoined for the examination on the merits. Thus, Claims 1, 4-19 and 21-23 are at issue and present for examination.

Applicants' arguments filed on 05/13/2008, have been fully considered, and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

Claims 1, 5, 10, 11, 15, 16, 21 and 23 are objected to because of the following informalities:

Claim 5 is objected to for reciting the phrase "selected from the group consisting essentially of…," which can be improved with respect to form. The reason is that the

phrase "consisting essentially of" is normally considered open language. As such, the phrase as written encompasses not only the quenchers recited but also unknown quenchers which are not listed in claim 5.

Claims 1, 10, 11, 15, 16, 21 and 23 are objected to for the use of terms "riboflavin photosensitizer," "riboflavin," and/or "photosensitizer" because these claims can be improved with respect to consistency. If Applicant's intended photosensitizer is riboflavin, the Examiner suggests replacing the terms with ---riboflavin acting as a photosensitizer---. The Examiner will use the suggested language for examination purposes.

Claim 21 is objected to for the recitation of "pathogen reduced" which can be improved with respect to form. The Examiner suggests replacing the noted phrase with ---pathogen-reduced---.

Claim 21 is objected to because the step of "damaging" can be improved with respect to clarity. The Examiner suggests inserting ---by--- so that the steps of "damaging" and "adding" recite ---damaging the nucleic acid of any pathogenic white blood cells, bacteria or viruses which may be present with the blood or blood components by adding riboflavin acting as a photosensitizer to the blood or blood components---. Without inserting "by" as suggested, the step of damaging is performed prior to adding riboflavin and exposing to UV/Vis. light, which defeats the purpose of adding riboflavin and exposing to UV/Vis. light.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 6, 9, 11-19, 22 and 23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 6, 9, 22 and 23 recite the limitation "the fluid" . There is insufficient antecedent basis for this limitation in the claims since there is no fluid recited in Claims 1 or 21.

Claims 11 (12-19 dependent therefrom) recites the phrase, “substantially maintaining the damage to the nucleic acids,” which is unclear. It is indefinite and unclear because the term “substantially” is a relative term and neither the claim nor the specification provides a standard for ascertaining the requisite degree. The term“ substantially maintaining” is confusing with respect to how long it has to maintain damage.

The previous rejection of Claims 1, 4-7, 9, 10 and 21-23 under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement, is withdrawn because the genus of riboflavin photosensitizers is well-known in the art.

The previous rejection of Claims 1, 4-7, 9, 10 and 21-23 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn because blood components are well-known in the art.

Claims 1, 4-19 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for a process comprising steps of: adding to a solution containing pathogenic white blood cells, bacteria and/or viruses, 50 μM of isoalloxazine comprising riboflavin; irradiating a solution containing said pathogenic white blood cells, bacteria and/or viruses, 50 μM of isoalloxazine with light, at wavelength of 320 nm and intensity of 7 J/cm^2, to activate isoalloxazine to cause single strand and double strand breaks to the deoxyribonucleic acids and ribonucleic acids of said pathogenic white blood cells, bacteria and/or viruses; wherein said strand breaks caused by the isoalloxazine and light, at wavelength of 320 nm and intensity of 7 J/cm^2, is maintained during storage of the solution after irradiation, does not reasonably provide enablement for [1] a process for *preventing self-repair* of nucleic acid of pathogenic white blood cells, bacteria and/or viruses which may be contained in blood components comprising the steps of: adding to the blood components a riboflavin photosensitizer; irradiating the blood components and riboflavin with light in a visible or UV range at an appropriate wavelength to activate the riboflavin to fragment the nucleic acid of the pathogenic white blood cells, bacteria and/or viruses to cause permanent damage to the nucleic acid; preventing self-repair of the nucleic acid; and wherein the permanent damage to the nucleic acid caused by the

photosensitizer and light is maintained over time such that the pathogenic white blood cells, bacteria and/or viruses will not reproduce in any blood component; [2] a process for inactivating white blood cells which may be contained in a fluid comprising: adding to the fluid containing white blood cells an effective amount of riboflavin; exposing the fluid and riboflavin to light of an appropriate wavelength to activate the riboflavin and cause damage to the nucleic acid of the white blood cells; and substantially maintaining the damage to the nucleic acids of the white blood cells *to prevent re-activation of the white blood cells*; and [3] a process for providing pathogen reduced *fluid containing blood or blood components suitable for re-infusion into a patient* comprising: damaging the nucleic acid of any pathogenic white blood cells, bacteria or viruses which may be present with the blood or blood components; adding riboflavin to the blood or blood components; and exposing the blood or blood components to UV or visible light to activate the riboflavin to fragment the nucleic acid of the pathogenic white blood cells, bacteria or viruses *to prevent them from reproducing* in the blood or blood components after re-infusion into the patient (italicized for added emphasis). Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 4-19 and 21-23 are so broad as to encompass any method comprising an irradiating step wherein an appropriate wavelength and intensity of light/UV is used to irradiate a fluid comprising blood components, i.e., red/white blood cells, platelets, etc, pathogenic white blood cells, bacteria and/or viruses, and riboflavin acting as a

photosensitizer, in order to prevent self-repair of nucleic acid damages resulting from the irradiating step so that re-activation of pathogenic white blood cells, bacteria and/or viruses and/or reproduction of pathogens is prevented. The enablement issue involving the claimed methods is whether or not the self-repair processes of all of the nucleic acid damages that result from the irradiating step can be prevented, or the re-activation of pathogenic white blood cells, bacteria and/or viruses and/or reproduction of pathogens is prevented.

Based on the fact that there are myriads of DNA repair processes, i.e., single strand break repair pathways, double strand break repair pathways via non-homologous end-joining, homologous recombination or single strand annealing, in addition to base excision, nucleotide excision, mismatch repair, and interstrand crosslink repair, to name a few, that work together to preserve the integrity of genomic DNA, which is vital for all life forms, it is unclear how the claimed methods can *prevent* the self-repair of the all types of nucleic acid damages that result from said irradiating step. Further, the redundancy of these repair pathways ensures highly discriminatory and efficient DNA repair mechanisms for the preservation genomic DNA in a mammalian cell so that if one repair pathway fails, another may be utilized to repair as many as 10,000 DNA lesions occurring in a metabolically active mammalian cell (see, Lindahl, T., Instability and decay of the primary structure of DNA. Nature, 362: 709-715, 1993). In support of this notion, the Figure 4 of the specification shows that not all cells are prevented from self-repair since the percentage of cells after treatment with either [1] UV in the presence of riboflavin stays at mere 36.1% in day 1, and 87.5% in day 2, or [2] visible light in the

presence of riboflavin stays at mere 44.6% in day 1, and 40.6 in day 2 (see 2nd and 4th lines in the table) ,which suggests that there is an ongoing repair of the nucleic acid damages. Taken together, one of skill in the art is not enabled from the limited disclosure of the specification as described above for a method of preventing self-repair of all types of nucleic acid damages in pathogenic white blood cells, bacteria and/or viruses resulting from said irradiating step so that re-activation of pathogenic white blood cells, bacteria and/or viruses and/or reproduction of pathogens are prevented.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the claimed methods, having the desired biological/chemical/physical characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 6-8, 11-14, 16-19, 21 and 23 are rejected under 35 U.S.C. § 102(e) as being anticipated by Goodrich et al. (USPN 6,258,577).

The rejection was stated in the previous office action as it applied to previous claims 1, 6, 7, 10, 21 and 23.

Applicants argue that the Goodrich reference does not expressly disclose the limitations in claims 1 and 21 that riboflavin and light fragment the nucleic acids of pathogens, preventing the pathogens from repairing themselves. There is no disclosure that this inability to self-repair prevents the pathogens from reproducing in the blood components.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. While Goodrich et al. do not specifically teach prevention of self-repair of nucleic acids from pathogenic white blood cells, bacteria and/or viruses, this limitation is inherent to the method disclosed by Goodrich et al. at least with regard to viruses as evidenced by applicant's specification. In support of this notion, in Figure 7 and page 14 of the specification, the lambda phage virus irradiated with 320 nm UVB at 0.08 J/cm^2 in the presence of 300 μM riboflavin concentration, was

not re-activated when it was incubated with E. coli host cells for 20 minutes to allow for viral absorption after the irradiation step. Therefore the method of Goodrich et al., which also requires the steps recited in the claims, would inherently result in prevention of self-repair of viruses. It is noted by the Examiner that Claims 8, 11-14 and 16-19 are included in this rejection for the same reasons as described herein and in the previous office actions. For the reasons provided herein and in the previous office actions, the rejection under this statute is maintained.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-8, 10-14, 16-19, 21 and 23 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Goodrich et al.[1] (USPN 6,258,577) in view of Goodrich et al.[2] (WO/2002/096471, VIRAL INACTIVATION PROCESS USING ANTIOXIDANT).

Claims 1, 4-8, 11-14, 16-19, 21 and 23 are drawn to [1] a process for preventing self-repair of nucleic acid of pathogenic white blood cells, bacteria and/or viruses which may be contained in blood components comprising the steps of: adding to the blood components a riboflavin photosensitizer to a final concentration of 50-500 μM;

irradiating the blood components and riboflavin with light in a visible or UV range at an appropriate wavelength to activate the riboflavin to fragment the nucleic acid of the pathogenic white blood cells, bacteria and/or viruses to cause permanent damage to the nucleic acid; preventing self-repair of the nucleic acid; and wherein the permanent damage to the nucleic acid caused by the photosensitizer and light is maintained over time such that the pathogenic white blood cells, bacteria and/or viruses will not reproduce in any blood component, optionally further comprising adding a quencher, i.e., glutathione, n-acetyl-cysteine, cysteine, adenine, histidine, tyrosine, tryptophan, ascorbate, vitamin E, trolox, alpha-tocopheral polyethylene glycol succinate (TPGS) and mixtures thereof, to the fluid; [2] a process for inactivating white blood cells which may be contained in a fluid comprising: adding to the fluid containing white blood cells an effective amount of riboflavin to a final concentration of 50-500 μM; exposing the fluid and riboflavin to light of an appropriate wavelength to activate the riboflavin and cause damage to the nucleic acid of the white blood cells; and substantially maintaining the damage to the nucleic acids of the white blood cells to prevent re-activation of the white blood cells; and [3] a process for providing pathogen reduced fluid containing blood or blood components suitable for re-infusion into a patient comprising: damaging the nucleic acid of any pathogenic white blood cells, bacteria or viruses which may be present with the blood or blood components; adding riboflavin to the blood or blood components to a final concentration of 50-500 μM; and exposing the blood or blood components to UV or visible light to activate the riboflavin to fragment the nucleic acid of

the pathogenic white blood cells, bacteria or viruses to prevent them from reproducing in the blood or blood components after re-infusion into the patient.

The teachings of Goodrich et al.[1] (USPN 6,258,577) are as described in the previous office actions and herein.

Goodrich et al.[2] (WO/2002/096471) teaches quenchers, glutathione, n-acetyl-cysteine, cysteine, adenine, histidine, tyrosine, tryptophan, ascorbate, vitamin E, trolox, alpha-tocopheral polyethylene glycol succinate (TPGS) that can be used in a method of inactivating pathogens in a biological fluid containing blood or blood products as well as pathogens comprising treating the biological fluid with a pathogen inactivating compound wherein the pathogen inactivating compound comprises riboflavin; adding to the biological fluid and riboflavin a quencher to reduce the level of side reactions without interfering with the inactivation of pathogens by riboflavin; and exposing the biological fluid and riboflavin and quencher to light to inactivate any pathogens contained in the biological fluid (see pages 44-48).

It would have been obvious to one of ordinary skill in the art to practice a method for decontamination of a fluid, by inactivation of microorganisms therein such that said fluid can be administered to a patient, said fluid containing a component selected from the group consisting of biologically active protein, blood, and blood constituents, without destroying the biological activity of such components, said method comprising: (a) adding an effective, non-toxic amount of riboflavin to said fluid; (b) exposing the fluid of step (a) to UV or visible light to activate the riboflavin to cause damage to the pathogen nucleic acid as taught by Goodrich et al.[1], and add a quencher such as glutathione, n-

acetyl-cysteine, cysteine, adenine, histidine, tyrosine, tryptophan, ascorbate, vitamin E, trolox, alpha-tocopheral polyethylene glycol succinate (TPGS), as taught by Goodrich et al.[2]. One would have been motivated to practice such methods because it is important to quench the side reactions that are produced by exposing the blood components to photosensitizer such as riboflavin and UV/VIS light (see page 5, line 21 to page 6 of Goodrich et al.[2]). One would have had a reasonable expectation of success to practice such methods because the use of quencher taught by Goodrich et al.[2] was in the methods that were almost identical to the methods taught by Goodrich et al.[1].

Double Patenting

The filing of a terminal disclaimer over claims 1-18 of the Goodrich patent is acknowledged. It is noted by the Examiner that said terminal disclaimer filed on 08/06/07 has been approved. Therefore, the rejection under this statute is withdrawn.

Conclusion

Claims 1, 4-19 and 21-23 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in this Office action to be fully responsive in prosecution.

This office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on M-F between 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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